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Lin Entry 1 of 1

Filter William

241

US-PAT-NO: 62:4533

DOT MENT IDENTIFIER: NO 62841 - PI

TITLE: Ilasmid-based valuine ion thesting atherosclenosis

DATE-ISSUED: September 4, 21 1

INTERNICH - INFORTION:

MARIE

.

HIF HAR HANTRY

Thomas; Lawrence J.

MAEdst.

US-TU CURRENT: <u>435 A. ...; 435 455</u>, 435 48<u>....</u>, <u>514 44</u>, 536 <u>23...., 186 23..4</u>, <u>536</u> 33... CLAIMS:

What is slaimen is:

- A DNA immuno period composition, comprissing a nucleotide sequence coding for an immunogenic polypeptide, which hadlestile sequence includes at least she segment odding for a B sell epitope of cholesteryl exten transfer protein. ETF linked in frame with an least she segment coding for a broad range helper T sell epitope, which muslestide segment is operably linked to a promoter requesive suitable for direction the transcription of the modestide sequence in a numbalian sell.
- 2. The INA immunosenta composition assording to claim a wherein said at least one segment coding for a B cell epitope of CETI encodes a B cell epitope of human CETI and consists of 5 A consecutive amino abids of SE(II NO:4.
- 4. The 1NA immunosemic composition according to claim I wherein said B rell epitope comprises a carboxyl terminal region of CET1, involved in neutral limid Binding or neutral ligid transfer activity.
- 4. The INA immunispenie com Orition are spirit to claim to different the helier f well epitope comprises a helper T cell epitope chialned from an antimento pertide selected from the group consisting of testands timoid, diphtherna tomin, pertussis vaccine, Basile Jalieste-Buerin BOT, polic vaccine, measles vazdine, mamps varrine, rubella vardine, purified pi telm derivative (i tuberrulin, Reyhole linget hen syanin, and otheristichs thereft.
- In The ING immunitarily typesetten and rains to claim i digress the immunipense polypeptide in Chaes two Bosel epitique of CFTE.
- The INA irran denic composition according to glain to which includes a rive segment in dinario material abids about the self-470 or SE, II II may and a 1894. when the final torum in a control of the fine will be self-in the au-
- To The 1974 immunitarity of project in some rains to collain to which in the body in the comment of find the agric of the association for the first in the 4 and 4 into

- The INA impair penish one within a containing to claim 1, where in wall at least the segment of dring for a relation to helper I well epitage encodes amind active fithrough 15 of JEQ II Not T.
- 9. The INA immunogenia composition according to claim 1, wherein said nucleotide sequence coding for an immunogenia polyperoide encodes the amino and sequence of SEQ II NOT.
- 1 . The DNA immunitarity imposition appurates to claim i, wherein the promoter is a sytumegalousity immediate early promoter wihabout.
- A 1NA immunitarity conjugation comprising a nucleatial arguence comprising.
- a an immediate early promoter enhancer region of sytomegalovirus SMM , operably linked to
- who a structural INA segment encoding an immunogenic polypeptide and comprising:
- i la INA se ment encoding amino acids i trivogh it will Expli NG: ",
- into a INA segment en oding amino acida 400 through 478 bf RE, Il No: 4, and
- iii a INA segment encoding amino acids :4% through :60 of SE, II NO: 4,
- which IMA segments i , ii and iii are linked in frame.
- 12. A DNA immunodenic composition comprising & nublective sequence comprising:
- an immediate early promoter enhancer region of cytomegalovirus CMV , operably linked to
- The approximate INA we ment encoding an immunopence polypeptide and comprising:
- in a INA segment encoding amino abids & through it will be; II NO: ",
- in la INA semment enfoding amin, avids 4-1 through 400 of SE, II NO: 4, and
- ill a INT. weiment entraint arthal wards (4% thickshow? of SEQ II NO: 4).
- which FNA segments is, -ii and iii are linked in frame.
- If. A INA immunogenic composition comprising a nucleotide sequence comprises a first seament an immunogenic polypeptide, which nucleotide sequence comprises a first seament coding for a broad range helper I cyll epitupe linked in frame with a second segment coding for a first B cell epitope of challestely ester transfer protein CETF having the nucleation requence of nucleotide tries of through III of SEQ II Notified at third seament ording for a second bound of curl epitipe of CETF having the nucleotide sequence of midlentides ill through IF correctly II Notified to a promote a ding for the immunocentry objective is operably linked to a promoter sequence cuit alle for directing the transcription of the nucleotide sequence in a manualish cell.
- 14. The INA production, to graph out to a condition to claim is wherein the above true we pend on a graph of the physical rule copies on the ${\mathbb R}^2$.
- If a All Mainmann tenir composition or spin in a unified to be dependent financial and in the principal support a position of the principal support of the principal suppor

- CETF having the naglestine ampende is nathestined. Which will I I is WE, II NOTE and a third segment of intribute a resond is well epithpe of CETF having the nucleatide sequence of intributions limit through 14.5 or WE, II NOTE, wherein the nucleatide sequence coding for the immunogenic polymetride is operably linked to a promotor sequence authable for directing the transcription of the nucleotide sequence in a mammalian sell.
- 18. A TIWA immunity-min composition comprising a numbertide sequence coding for an immunopenic polypeptide, which numbertide sequence comprises a first degment coding for a broad range helper T cell epitipe linked in-frame with a second segment coding for a first B well epitipe if tholesteryl ester transfer protein CETF having the numbertide sequence of numbertides 1945 through 1941 of SEL ID NOTS and a third segment roding for a second B cell epitope of CETF having the numbertide sequence of numbertides 1941 through 1425 of SEL ID NOTS, wherein the numbertide sequence coding for the immunopenic polypeptide is operably linked to a promoter sequence unitable for directing the transmitten of the numbertide sequence in a mammalian cell.
- 17. A TNA immunogenic composition comprising a nucleotide sequence being operably linked to an immunogenic polypeptide, said nucleotide sequence being operably linked to a promoter sequence suitable for directing the transfrigition of said nucleotide sequence in a manufalian cell, said immunogenic polypeptide comprising a B cell epitope portion, wherein said B cell epitope portion comprises at least one B cell epitope of cholesteryl ester transfer protein. CETP , and a broad range helper T cell epitope portion comprises at least one broad range helper T cell epitope.
- 19. The FMA immunogenic composition as sording to claim 19, wherein said at least one B cell epitope of CETF consists of δ -Le consequtive amino acids of SEQ II NO:4.
- 19. The PNA immunowence composition appoiding to plaim 17, wherein said at least one broad range helper T cell epitope is a broad range helper T cell epitope obtained from an immunogenic pertide selevied from the group consisting of terange toward, dightheria tumin, pertubbis variance, Basile dalmette-Savin Bos , pulso varrane, measless varrane, rungs varrane, rubella varrane, purified protein derivative of tubersulin, and summations thereof.
- do. The INA immunicating composition advarding to claim 17, wherein said immunicating polygentide includes two B well epitypes of CETE.

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Int Entry 1 of 1

File: SHT

gran 11, 27, 2

MS (AT-MO: 6412020 DOT MENT-IDENTIFIES: MS (410.00 B)

TITLE: Modelation in chilestoryl exter transfer fractein (TETH activity)

DATE-ISSUED: June 1:, 1 .1

INTENTOR - INFORMATION:

MAN Entre shows; Charles W

CONTRA .::::::

 $M_{\rm ch}$ Malden

US CI-CURRENT: 424 198.1; 424 100.1, 424 192.1, 424 192.1, 424 193.1, 424 196.1, 424 234.1, 581 381, 580 324, 581 418

CLAIMS:

1 31316:

- An isolated antigeria hybrid peptide orphizing a helper T cell epitope portion linked to a B cell epitore portion, wherein said b sell epitore portion Comprises six to le consécutive amino acids of the carboxyl terminal 20 arids of human cholesteryl exter transfer protein (SEQ II NO:1).
- ... The isolated antigenious principertide of siding to common wherein the helper Totell epitope portion is selected from the group consisting of a helper Theell epitope amino abid so paence of terminas toward, diplotheria toward, pyrtussis vandine, Badile dalmette-Guerin BDG , polid vaddine, measles vaccine, mumps vagoine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet nemocyanin, and vmichations thereof.
- The isolated antigenic hybrid peptide according to claim ., wherein the helper T cell epitope poition comprises a helper T cell epitope from tetanus taraid or digitheria tordid.
- 4. An isolated untipensy bybrid peptide typ rising the duing acid sequence of SE, II NO: N.
- 9. The isolated antigeniolighted peptide according to claim 4 statistics of the amine acid september of AE, II Notice
- The laglates antigenis hyrild peptines is faidify to clotted, therein said insplated antimenic hybrid poptide is a liner wildEQ II Notice
- 7. A massime symposition objection man anti-entry variance lighted populate. comprisent a universal neaper Totall equipe linker to a Botal epit pe point de communitation of the communitation and arrage in home, on legional so the primary telling retains 200. II fill it is
- organition is computed by a switch in the neighbor 100 la seritore roatri no i the antoenic marche byforic pertie is so selected in bothe

- from the lating of the abin and the pence of abin and the spin terms and the abin and sequence of abin, and the abin and sequence of abin, and the abin to be of tetangent to be of Eq. II NO. 3.
- For the varrine composition according to claim T wherein the T dell epitope portion of the antigenic varrine hybrid peptide is a universal helper T dell epitope selected from the group consisting of T dell epitope amino acid sequences of tetanus toxoid, diphtheria toxoid, perfussis vaccine, Barile Calmette-Guerin BCS, polic vaccine, measles vaccine, mumps varrine, rubella vaccine, purified protein derivative of taker culin, keynole limget hemosyanin, and combinations therest.
- il. The vargine gumposition arbording to glaim T wherein the antigenic vargine hybrid pertide further comprises an amino terminal systeme residue.
- ii. A method of elevating the ratio of diroulating High Lensity Lipoprotein to biroulating Low Lensity Lipoprotein, Very Low Lensity Lipoprotein, or total cholesterol in a human or other animal comprising administering to the human or animal an antigenic vacuine hybrid peptide comprising a universal helper T cell epitope portion and a F cell epitope portion, wherein said B cell epitope portion comprises six to 2. Consecutive amino acids of human cholesteryl ester transfer protects. SEQ MI NO:1.
- 12. The method apporains to slaim if wherein the helper T cell epitope portion of the antigenic vaccine hybrid peptide is selected from the group consisting of the amino acid sequence of amino acids 60% to 640 of totanus toxin protein amino acids 2 to 15 of SE2 IC MO:2 and the amino acid sequence of amino acids 947 to 967 of tetanus toxin protein SE2 IC MO:3 .
- 13. The method according to glaim II wherein the antigenic vaccine hybrid peptide further comprises an amino terminal systems residue.
- 14. A method of decreasing the level of diclostery lester transfer protein activity in a human or other animal comprising administering to the human or animal an antigence varying hybrid pepting officials a helper T cell epitipe portion opposition as at to 16 consequence aming acids of the carboxyl terminal Decaming acids of human englesterol ester transfer protein (SEQ II NO:1).
- 15. The method according to claim 14 wherein the antigenic vagoine hyprid peptide is administered in an amount sufficient to elicit production in said human or other animal of anti-cholesterol ester transfer protein antibodies.
- lé. A méthod of increasing the level of diroulating High Lensity Lipoprotein in a human or other animal comprising administering to the human or animal an antisedic vagothe hybrid peptide campiling a helper I cell epitope portion and a B cell epitope portion, wherein said b cell epitope portion comprises six to de consecutive amino asids of the carbonyl terminal de amino asids of human cholesterol ester transfer protein. SE, II Nov.
- 17. The method a coordinate glaim le, wherein the helper T sell epitops portion is delegated from the group Consisting of Universal helper T cell epitope amino acid sequences of tetoms toward, diphaleria toward, pertussis yaccine, Basile Calmette Sperin BCS, polic vascine, measles yaccine, numps vascine, rubella vascine, purified protein derivative Di tuber culin, keyl le limpet hemoryanin, and combinations there is
- If. A method of treating atheres derivation of human or animal comprising autimistering to the number of duminous and interest to a transfer a pertident of principle and investigation of the second of the pertident of the second of the transfer of the second of the se

- in the method and rules to any one if claims 11, is, in, indir, wherein said antidents vacaine hybrid peptide is a dimer.
- 1). A method of making an anti-cholesteryl ester transfer protein. CETF vaccine comprising a B cell epitope portion and a helper T cell epitope portion to modulate endopenous sWTF activity, comprising:
- sale-ting a B cell epitope portion from a region of 'ETF involved in neutral limid binding or neutral limid transfer activity;
- selecting a helper T cell epitope portion consisting of a helper T cell epitope; and
- linking said B cell epithpe portion and said helper T cell epitope portion to form a single immunogenia molecy.
- 2). The method ambording to claim 20 wherein said B cell epitope portion is covalently linked to said helper T cell epitope portion.
- 22. The method as widing to claim 21, wherein usid 8 cell epitope portion is somalently linked to said helper T cell epitope portion via a covalent bond selected from the group consisting of pertide bonds and disulfide bonds.
- 23. The method according to blaim 21 wherein said B cell epitope portion is linked to said helper T cell epitope portion via a cross-linker molecule.
- 24. The method appointing to claim 2, wherein said H well epitope portion is linked to said helper T well epitope portion via a bridge of amino acids.
- 15. The nethod as writing to blaim I' wherein haid B hell epitope portion and said helper T bell epitope portion are linked to a sommon partier molecule.
- 20. The method a wording to plaim 21 therein vard H well epitope portion is linked to said helper T well epitope portion to form a valuence peptide and further comprising the step of linking gaid varbine peptide to a garrier molecule.

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Lit Entry 1 at 1

File: TETT

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DOCTMENT: DÊNTÎPIÊR: DO GEFFIIS FI

TITLE: Modulation of chalesteryl ester transfer protein (ATI) autivity

DATE-ISSUED: April 19, 10.5

INVENTOR INFORMATION:

NAME STATE TO THE CONTROL

Firtershaus; Charles W. Malden MA Thomas; Lawrence J. Wordester MA

US-CL-CURRENT: 484 188.1; 484 146.1, 424 186.1

CLAIMS:

What is claimed is:

- I. A method of elevating the ratio of diriculating HIL to direculating LIL, VIII, or total cholesterol in a human or other animal comprising administering to the human of animal a vascine compliantion comprising a pertude consugate complising a helper Tuelf epitope portion linked to a Burell epitope portion, wherein data Burell epitope portion comprises a burell epitope of a SETE of a human of other animal, and said pertude consumate, when administered to said human of other animal, elicits production of endopenous antibodies that specifically bind endopenous CETE and results in an elevation of the ratio of circulating HTL to directating LTL, VIIIL, or total dislostered to said human or other animal.
- I. A method associding to claim 1 wherein said is cell epitape portion comprises between six and IV consecutive amino acids of the sailongl terminal 26 amino acids of human CETP SEQ IT NO:1 .
- The method absording to claim I wherein the helper Totall epitope portion of the peptide computate compilses a Totall epitope selected from the group consisting of the amino abid sequence of amino abids of two 64s of retunds town protein lamino Acids Totals of SE, II Not and the amino acid sequence of amino acids of two 60st tetalus town protein of SE, II Note.
- 4. The nethed approximate of and a wherein the Eurell epitope portion of the peptide formulated is selected from the most observation of Fetween six and decompositive animal acids of SE, II North
- The method arrow differ to black I wherein the perturbation which harries improves an aming terminal by teams red Rev.
- A method for reacting the level of end send of WTE attractly in a human of their animal of product a minustering to the human or animal appetite the drafter outproduct a heaper Total aproper part, in linear to a Forell epit per part in outproduct a Forell epit sector. WTE of a number animal, wherein call poptities on drafter who a amount term is to a administer animal, educate.

- production of end send and into these that operativally bind endopenous SETE and results in a desirace in the level of end genous SETE activity in said human or animal.
- 7. The method according to claim 4 wherein the peptide gangupate is administered in an amount sufficient to eligit production in said human or other animal of anti-CETP antibodies.
- e. A method of altering the masabblish of HTL-cholesterol to debrease the development of atherosoleratic lesions in a human of other animal comprising administering to the human of animal a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, said helper T cell epitope portion comprising a Froad range T cell epitope and said B cell epitope portion comprising a B cell epitope of CETE, wherein said peptide conjugate, when administered to said human of animal, elicits production of endogenous antibodies that specifically bind endogenous CETE and results in a decrease in the development of atherosolerotic lesions in said human or animal compared to a human or animal not receiving such treatment.
- F. A method of increasing the level of circulating Hill in a human or other animal comprising administering to the human or animal a pertide congugate comprising a helper T bell epitope portion and a B well epitope portion, wherein said B bell epitope portion comprises a B well epitope of a CETP of a human or other animal, and wherein said peptide congugate, when administered to said human or animal, elicits production of endowenous antibodies that specifically bind endogenous CETF and results in an increase in the level of circulating HTL in said human or animal.
- 1. The method according to claim 9, wherein the helper T cell epitope portion comprises a helper T cell epitope derives from an antigenic peptide selected from the group consisting of tetanus toward, diplitheria toward, pertussis vascine, Habile Calmette-Suerin BC3, polic vascine, measles vascine, mumps vascine, rubella vaccine, purified protein defivative of tuberculin, keyhole limpet hemogramin, and comminations thereof.
- 11. The method afrômaing to claim by offerein the Borell epitope portion comprises a carboxyl ferminal region of human CETF consisting of between six and Decompositive amino acids of SE, II NOTE.